03 Issue 3 - 2017
December 2017

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

What's new in Pharmacovigilance?

QPPV UPDATE

Published by the European Medicines Agency

An agency of the European Union

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QPPV Update

This last Issue of 2017 provides you with information on recent developments in EU Pharmacovigilance for medicines for human use, includes updates on the EU network activities, **with a particular focus on the launch of the new and improved version of EudraVigilance**.

We wish you a Happy Christmas and New Year and look forward to continued collaboration in 2018.

Need more information?

Further information about the work of the European Medicines Agency is available on our website

For topics on Pharmacovigilance legislation – see here

Links to the National Competent Authorities can be found here

Pharmacovigilance IT Systems

EudraVigilance

The new EudraVigilance system was launched on 22 November 2017

Major achievements in 2017

- The fieldwork of the independent audit of the EudraVigilance (EV) functionalities agreed by Pharmacovigilance Risk Assessment Committee (PRAC) and the EMA Management Board (MB) took place in February and April 2017.
- Based on the independent audit report and on a favourable recommendation from the PRAC, on 22 May 2017 the EMA MB confirmed that the EudraVigilance system had achieved full functionality and the system meets the functional specifications that were adopted by PRAC and Board in December 2013 (announcement of the EMA Management Board).
- Testing with national competent authorities (NCAs) and stakeholders was initiated on 26 June 2017 following the release of the new EudraVigilance test environment (XCOMP). This allowed organisations to become familiar with the new system and to test their local pharmacovigilance IT system and their interoperability with the enhanced EV system.
- The registration process for marketing authorisation holders (MAHs) to access the EudraVigilance data analysis system (EVDAS) was launched on 1 June 2017. By 6 December 2017, access to EVDAS had been granted to 6266 EV users. In total, 8831 new EV users and 560 new organisations were registered in EudraVigilance by 6 December 2017.
- Based on the agreed EudraVigilance training plan, EMA published e-learning modules and technical documentation including user manuals, a revised change management plan and a Question and Answer document. In addition, EMA organised 41 stakeholder webinars including national competent authorities (NCAs), MAHs and sponsors of clinical trials.
- Twenty-seven EudraVigilance and E2B(R3) Individual Case Safety Report (ICSR) submission face-to-face training courses were organised in 2017. For EudraVigilance training courses, please visit the EudraVigilance training page.
- To assist MAHs in preparing for the go-live of the new EV system, the Agency released a 'Checklist and testing instructions for MAHs and Sponsors of Clinical Trials in the EEA'. This document provided some general testing instructions, easy to follow steps to assist MAHs and sponsors in preparing for the technical and business process changes.
- On 4 October 2017 further instructions, including detailed information on measures which were put in place by organisations during the EudraVigilance downtime, were published as part of the EudraVigilance go-live plan and the Technical Note. The plan outlined the tasks and activities required to launch the new EudraVigilance production system and explained the process for handling the legacy data resulting from the downtime and described temporary arrangements. The go-live plan also highlighted the mechanisms in place to notify any emerging safety issues by MAHs or sponsors of clinical trials to NCAs and the EMA.
- **On 22 November 2017, EMA launched the new and improved version of EudraVigilance** with enhanced features for reporting and analysing suspected adverse reactions related to medicines (New EudraVigilance system is live). Together with the launch, further legal obligations became applicable to the mandatory electronic reporting through EudraVigilance, as stated in the announcement of the EMA Management Board, published in May. This is an important step forward, improving public health protection through monitoring the safety of medicines. This milestone is important for the EU and beyond, as the EU contributes to global safety monitoring. The operational benefits for regulators and stakeholders will provide a robust basis for pharmacovigilance and signal detection activities for years to come. The enhancements and expected benefits of the new EudraVigilance are:

New feature	Benefit
• Enhanced signal-detection and data-analysis tools to support safety monitoring directly by Member States and marketing authorisation holders	• Better detection of new or changing safety issues, enabling rapid action to protect public health
• Improved quality and completeness of ICSR data	• Better searchability and more efficient data analysis
• Enhanced scalability of the EudraVigilance system	• Able to support an increased number of ICSRs due to the new requirement to report non-serious cases to EudraVigilance
• Simplified reporting of ICSRs to EudraVigilance and the rerouting of ICSRs to Member States	• Reduced duplication of efforts • Marketing authorisation holders no longer have to provide ICSRs to national competent authorities: they have to submit these to EudraVigilance only
• Provision of EU case reports to the World Health Organization (WHO) Uppsala Monitoring Centre directly from EudraVigilance	• Enhanced collaboration between EU and WHO • Member States will no longer need to carry out this task

What's coming

After the go-live of the new EudraVigilance system on 22 November, the EMA is engaged in the following activities:

- increased monitoring of the EudraVigilance system;
- enhanced user support by the EMA Service Desk;
- additional training courses on the use of EudraVigilance and ICSR E2B(R3) submissions in 2018;
- continuation of the monthly EudraVigilance support webinars for NCAs, MAHs and sponsors;
- additional release (release 5) in February 2018, to address any potential issues identified after 22 November 2017 (any downtime for release 5 is expected to be minimal and of a similar nature to previous routine updates).

What MAHs need to know and do:

- **From 22 February 2018, MAHs will be required to monitor EudraVigilance data for active substances included in the 'List of medicinal products under additional monitoring' and inform the Agency and national competent authorities of validated signals.** More information on the 'phased implementation' requirements to monitor EudraVigilance data can be found on the signal management webpage.

Pharmacovigilance Processes

Measuring the Impact of Pharmacovigilance Activities

What's new?

In November 2017 the revised PRAC strategy for measuring the impact of pharmacovigilance activities was published. The strategy aims to improve pharmacovigilance practices and determine which activities are most successful.
Building on previous achievements, the impact of major regulatory interventions will be evaluated by combining different methodologies that measure changes in knowledge and behaviour, trends in drug use, and changes in morbidity or mortality. This revision shifts the focus to activities and regulatory tools that make a difference for patients in daily healthcare.
To capture patient-relevant health outcomes the strategy will explore models for multi-stakeholder collaboration, reaching beyond medicines regulation in the four strategic areas:

- measuring real-world effectiveness of risk-minimisation measures;
- measuring impact of specific pharmacovigilance processes (e.g. post-authorisation safety studies);
- exploring ways for effective engagement with patients and healthcare professionals;
- development of and guidance on methodologies for impact research.

Pharmacovigilance Processes

EMA's first public hearing

What's new?

Patients, carers, doctors, pharmacists and academia shared their experience with valproate - a medicine that treats epilepsy, bipolar disorder and migraine - at the first public hearing held by the EMA on 26 September 2017.

The public hearing was held as part of a review of the safety of using valproate-containing medicines in women and girls who are pregnant or of childbearing age by EMA's Pharmacovigilance Risk Assessment Committee (PRAC).

The hearing gave an opportunity to EU citizens representing a wide range of groups to make their voices heard to complement the available scientific evidence in the evaluation of this medicine. The total number of attendees was 65, including 28 patients and patient representatives, 19 healthcare professionals and academics, 11 from pharmaceutical industry and 7 from media. More information on the deliberations made during the hearing can be found in the summary report. The hearing was broadcast live and the video recording can be found here.

What's coming?

The PRAC will take into account every single input received during the hearing. At the end of this review, the Committee will publish an assessment report on measures to reduce the risk of valproate-containing medicines during pregnancy and in women of childbearing potential, in accordance with the published timetable.

Pharmacovigilance in the product lifecycle

PSUR roadmap

What's new?

Following the Periodic Safety Update Report (PSUR) joint industry/assessor webinar training held on 22 September 2017, the explanatory note (EN) to Good pharmacovigilance practices (GVP) Module VII and the Questions and Answers (Q&A) for assessors have been updated to address questions raised during the training.

The updated documents include the following revisions:

- Update with regard to the safety concerns in the risk management plan (RMP) and in the PSUR as introduced by GVP Module V Rev.2 (pages 9-10 EN; page 7 Q&A).
- Information regarding the inclusion of EudraVigilance data in PSUR from monitoring of EudraVigilance by the MAH which came into force on the 22 of November 2017 (here) (pages 10-11 EN; pages 8-9 Q&A).
- PSURs should be submitted in English (page 2 of the EN).
- Follow-up to a PSUR Single Assessment (PSUSA) should be avoided when the PSUR cycle of an active substance or a combination of active substances is under or on a yearly basis (page 12 Q&A).

The previous versions of both documents were adopted by PRAC on 23 March 2017.

The updated documents are available on the PSUR EMA webpage.

Patient Registries Initiative

What's new?

The EMA's Patient Registries Initiative aims to expand the use of patient registries 'by introducing and supporting a more systematic and standardised approach to their contribution to the benefit-risk evaluation of medicines'. To explore the challenges and barriers for using patient registry data in regulatory evaluations, the EMA hosted workshops in June and July this year focusing on two areas currently very active in new drug development, Cystic Fibrosis and Multiple Sclerosis.

Participants included registry holders, marketing authorisation holders/applicants, patient representatives, regulators, and reimbursement and health technology assessment bodies. Focused work-group discussions resulted in recommendations on measures relating to common data elements, governance, data sharing and interoperability that should facilitate the systematic integration of registry data, where appropriate, in regulatory evaluations.

The Workshop Reports outlining the recommendations and actions to be implemented in each case are now published on the webpage of the Patient Registries Initiative here.

Pharmacovigilance guidance

Recently published guidance

- GVP Module VI – Management and reporting of adverse reactions to medicinal products (Rev 2), following the public consultation, was released as final on 2 August 2017.
- GVP Module VI Addendum I – Duplicate management of suspected adverse reaction reports was released as final on 2 August 2017.
- GVP Module VIII – Post-authorisation safety studies (Rev. 3) was released as final on 12 October 2017, following alignment with the recent Revision 2 of GVP Module VI on ICSR submission and management;
- GVP Module IX – Signal management (Rev. 1) and revised IX Addendum I – Methodological aspects of signal detection from spontaneous reports of suspected adverse reactions, following the public consultation, were released as final on 12 October 2017.
- GVP Module XV – Safety communication (Rev. 1) and related templates in Annex II (Direct Healthcare Professional Communication (DHPC) (Rev. 1), and Communication Plan for Direct Healthcare Professional Communication (CP DHPC) were released as final in October 2017, following the public consultation.
- GVP Annex I - Definitions (Rev. 4) was published as final on 12 October 2017. The annex has been updated with the new definitions from legislation and revised GVP Modules, and for supporting future application of revised definitions introduced by Clinical Trial Regulation (EU) No 536/2014.
- GVP Annex V – Abbreviations (Rev. 1) was published as final on 12 October 2017.

Guidance under revision or development in 2018

- The pharmacovigilance guideline for paediatric medicines is being finalised as a chapter of GVP, following the public consultation completed in 2017.

The revision and development of other guidance in 2018 and beyond is being reviewed in light of preparation for the Agency's relocation as a result of the UK's exit from the EU and its impact on the Agency's business continuity, and may be subject to further review and reprioritisation in accordance with the business continuity plan of the Agency.

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union